Animal model for detrusor underactivity following radical pelvic surgery with nerve-sparing technique by crushing injury of nerve bundles from major pelvic ganglion to the bladder

Hypothesis / aims of study
Voiding dysfunction such as incomplete emptying and urinary retention is a common complication after radical pelvic surgery and the voiding dysfunction is highly associated with the low quality of life (QoL) after surgery for pelvic malignancy. Therefore, the nerve-sparing radical pelvic surgery had been introduced to reduce voiding complication. Nonetheless, some patients experienced voiding dysfunction although they were treated with the nerve-sparing radical pelvic surgery. Therefore, it is necessary to understand physiology of voiding dysfunction after nerve-sparing radical pelvic surgery using representative animal model. In this study, we evaluated the functional, morphologic and molecular changes of the bladder in animal with voiding dysfunction after injury which is represent of nerve damage during nerve-sparing radical pelvic surgery.

Study design, materials and methods
Male Sprague Dawley Rats (SD rats) were used: normal rats (Group I, n=5), sham-operated rats (Group II, n=5), rats with bilateral crushing nerve bundles from Major pelvic ganglion (MPG) to bladder (Group III, n=10). After 1, 2, 4-week, bladder muscle strip were prepared and the contractile responses were evaluated. And then, the bladder was collected. Masson-trichrome staining was done to evaluate the smooth muscle to collagen ratio. Western blot analyses with M3 receptor subtype, M2 receptor subtype, and RHO were done in the bladder.

Results
After crushing injuries of nerve bundles from MPG, bladder contractility tended to be significantly decreased at 1-week after the injury, and then, the decreased bladder contractility was continued at 4-week. At 1-week after injury, significant increased bladder weights in rats with crushing nerve injury were begun and maintained at 2- and 4-week compared with normal rats. Histologic analysis showed that the mild decreased smooth muscle-to-collagen ratio of bladder wall was observed in rats with the crushing nerve injury but the change was not significant compared with normal rats at 1-week after injury. However, the smooth muscle-to-collagen ratio of bladder wall in rats with crushing nerve injury was significantly decreased from 2-week after injury. After 4-week, the expression of M3 receptor subtype was decreased however, there was no significance compared with the sham-operated rats. The expression of M2 receptor subtype and RHO was significantly increased compared with the sham-operated rats.

Interpretation of results
After crushing injuries of nerve bundles from MPG, decreased bladder contractility, increased bladder weight, and decreased smooth muscle content in the bladder were observed and these results were reliable finding as detrusor underactivity following crushing nerve injury. M2 receptor subtype and RHO might have more important role than M3 receptor subtype after crushing nerve injury. Although the expression M2 receptor subtype was significantly increased after crushing nerve injury, the decreased bladder contractility was observed. Therefore, the Rho-kinase pathway may be the more important to control the detrusor contractility.

Concluding message
Crushing injury of nerve bundles form MPG to bladder induced morphologic, histologic, and molecular changes of bladder. And the decreased bladder contractility after crushing nerve injury in the rat seemed to be reliable with the voiding dysfunction such as incomplete emptying following nerve-sparing radical pelvic surgery. In addition, Rho-kinase pathway may have the more important role to modulate bladder contractility than the M2 and M3 muscarinic receptors after crushing nerve injury. Based on these results, the animal model in this study can be apply to the study about the prevention and treatment of voiding dysfunction after nerve-sparing radical pelvic surgery.

References

Disclosures
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